Evaluating Preprocessing Choices in Single-Subject BOLD-fMRI Studies Using Data-driven Performance Metrics.

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INTRODUCTION. We tested the impact of spatial smoothing, within-subject alignment, and temporal detrending in BOLD-fMRI using prediction and reproducibility data-driven performance metrics from cross-validation resampling within the NPAIRS (**N**onparametric, **P**rediction, **A**ctivation, **I**nfluence, **R**eproducibility re**S**ampling) framework [1].

METHODS. Data Acquisition: Sixteen right-handed volunteers performed two runs of a static force task [2] alternating six rest and five force periods/run (44 s/period; 200-1000 g randomized forces with thumb and forefinger). Data collection used a Siemens 1.5T clinical scanner (fMRI:EPI BOLD, TR/TE=3986/60 msec, FOV=22x22x15 cm, slices=30, voxel= 3.44x3.44x5 mm; MRI: T1-weighted 3D FLASH). **Preprocessing:** (i) Spatial smoothing/slice with a 2D gaussian kernel (FWHM = 0, 1.5 or 6 pixels). (ii) No within-subject registration or AIR3's six-parameter rigid-body transformation (AIR_6P, [3]); all scans were resampled into a reference MRI space. (iii) Temporal detrending using a linear combination of cosine basis functions (0, 0.5 or 2 cycles). **Analysis:** After a PCA of each run's scans a canonical variates analysis (CVA: two-class = force and rest brain states) with one of five levels of model complexity (number of PCs used) produced model parameters including a discriminant eigenimage. The NPAIRS framework uses split-half cross-validation resampling (ie. equal sized test and training sets), and for each subject each run was treated as both a training- and test-set. Average-prediction (p) and reproducibility (r) metrics per subject were generated by using the CVA parameters for one run to predict the brain state per scan in the other run, and by correlating the two eigenimages to produce r-values that are monotonically related to reproducible activation SNRs [1,4].

RESULTS AND DISCUSSION. For the average across all sixteen subjects, Fig. 1 plots prediction vs reproducibility curves as a function of model complexity for each combination of preprocessing choices. As in an ROC analysis, there is one optimal graph location: the ideal data set and analysis should provide perfect prediction and reproducibility (p,r) = (1,1). All curves depict a tradeoff between reproducibility, the match to the experimental design structure (prediction), and model complexity (degrees of freedom). For the upper six curves, alignment and some temporal detrending interact with spatial smoothing and are almost always beneficial, while more complex models tend to converge toward higher prediction with a large decrease in reproducibility. This indicates the decreased reproducible SNR expected as we obtain more accurate (i.e., less biased) prediction estimates with increasing model complexity, i.e., a bias-variance tradeoff. Optimal preprocessing choices are obtained with heavy spatial smoothing, implying that optimization must be performed as a function of spatial scale (e.g., Gaussian smoothing kernel size). Using a new data driven alternative to ROC curves we have shown that preprocessing choices are critical in optimizing fMRI data analysis approaches.

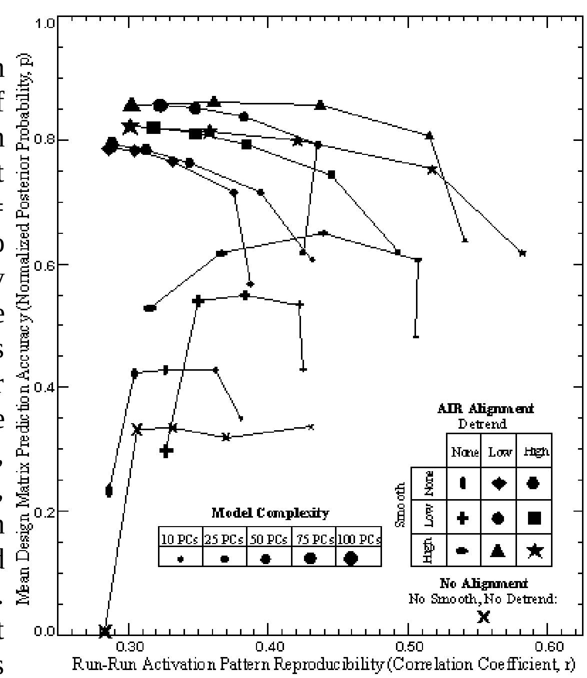

Figure 1. Each curve represents the average results from 16 subjects for a combination of smoothing, alignment, and temporal detrending choices analyzed with complex to simple models (left to right/curve). A curve's position and shape illustrates the tradeoffs between reproducibility of activation pattern SNR (r), match to experimental design (p), and model complexity.

REFERENCES. (1) Strother SC, et al., Neuroimage, (submitted). (2) Muley SA, et al., Neuroimage, (in press). (3) Woods RP, et al., J Comput Assist Tomogr, 22:139-152,1998. (4) Kjems U, et al., Neuroimage, (submitted).

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